

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US05/003061

International filing date: 01 February 2005 (01.02.2005)

Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/545,196
Filing date: 17 February 2004 (17.02.2004)

Date of receipt at the International Bureau: 03 March 2005 (03.03.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)



World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse

1286085

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

February 16, 2005

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: 60/545,196

FILING DATE: *February 17, 2004*

RELATED PCT APPLICATION NUMBER: *PCT/US05/03061*



Certified by

Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office



Attorney's Docket No. JJA-0305

Family Number P2004J007

"PATENT"

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Michael Siskin et al

For: SYNTHESIS OF STERICALLY HINDERED SECONDARY AMINOETHER ALCOHOLS
FROM ACID ANHYDRIDE AND/OR ACID HALIDE AND SULFUR TRIOXIDECommissioner for Patents
Mail Stop: Provisional Patent Application
P.O. Box 1450
Alexandria, Virginia 22313-1450322856 U.S. PTO
60/545196

COVER SHEET FOR FILING PROVISIONAL APPLICATION (37 C.F.R. § 1.53(c))

CERTIFICATION UNDER 37 C.F.R. 1.10 *

(Express Mail label number is mandatory) (Express Mail certification is optional)

☒ "Express Mail" mailing label number E U 8 6 3 1 0 0 7 8 9 U S . Date of Deposit February 17, 2004

I hereby certify that this correspondence and the documents referred to as attached therein are being deposited with the United States Postal Service, on the date indicated above, in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and is addressed to the Commissioner for Patents, Mail Stop: Provisional Patent Application, P.O. Box 1450, Alexandria, Virginia 22313-1450.

KATHLEEN A. KUNA

(TYPE OR PRINT NAME OF PERSON MAILING PAPER)

(SIGNATURE OF PERSON MAILING PAPER)

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 C.F.R. § 1.53(c):

- The following comprises the information required by 37 C.F.R. § 1.51(c)(1):
- The name(s) of the inventor(s) is/are:

1. Michael
GIVEN NAME- -
MIDDLE INITIAL OR NAMESISKIN
FAMILY (OR LAST) NAME2. Alan
GIVEN NAMERoy
MIDDLE INITIAL OR NAMEKATRITZKY
FAMILY (OR LAST) NAME3. Kostyantyn
GIVEN NAMEMykolayevich
MIDDLE INITIAL OR NAMEKIRICHENKO
FAMILY (OR LAST) NAME4. Adeana
GIVEN NAMERichelle
MIDDLE INITIAL OR NAMEBISHOP
FAMILY (OR LAST) NAME5. Christine
GIVEN NAMENicole
MIDDLE INITIAL OR NAMEELIA
FAMILY (OR LAST) NAME

27810

PATENT TRADEMARK OFFICE

Family Number: P2004J007

1. 56 Shongum Road, Randolph, New Jersey 07869, USA
2. 1221 Southwest 21st Street, Gainesville, Florida 32601, USA
3. 999 Southwest 16th Avenue, Gainesville, Florida 32601, USA
4. 2563 Costa Mesa Circle, League City, Texas 77573, USA
5. 437 Garretson Road, Bridgewater, New Jersey 08807, USA

- SYNTHESIS OF STERICALLY HINDERED SECONDARY AMINOETHER
-
- ALCOHOLS FROM ACID ANHYDRIDE AND/OR ACID HALIDE AND SULFUR
-
- TRIOXIDE

- | | | | |
|-------------------------|----------------|---|-----------------------------|
| Name of Attorney(s): | Norby L. Foss | / | Paul E. Purvin |
| Registration Number(s): | 47,571 | / | 29,203 |
| Telephone Number(s): | (908) 730-3644 | / | (908) 730-3618 |
| Customer Number | 27810 | | Deposit Account No. 05-1330 |

- The name of the U.S. Government agency and the Government contract number are:

- ☐ Other: _____

Attorney's Docket No. JJA-0305

Family Number: P2004J007

9. Fee

The filing fee for this provisional application, as set in 37 C.F.R. § 1.16(k), is \$ 160.00 for other than a small entity.

10. Method of fee payment

☒ Charge Deposit Account No. 05-1330 in the amount of \$ 160.00.
A duplicate of this Cover Sheet is attached.

Date: 16 Feb 2004


Signature of Attorney

Address to which correspondence is to be sent:

ExxonMobil Research and Engineering Company
P. O. Box 900
Annandale, New Jersey 08801-0900

PAUL E. PURWIN

Name of Attorney

Registration No.: 29,203

Telephone No.: (908) 730-3618

Facsimile No.: (908) 730-3649

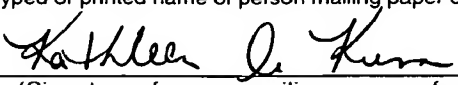
ALLOCCA:kak
2/16/2004

- a -

APPLICATION FOR UNITED STATES PATENT

SYNTHESIS OF STERICALLY HINDERED SECONDARY
AMINOETHER ALCOHOLS FROM ACID
ANHYDRIDE AND/OR ACID HALIDE AND SULFUR TRIOXIDE

Applicants: Michael Siskin
Alan R. Katritzky
Kostyantyn M. Kirichenko
Adeana R. Bishop
Christine N. Elia

"EXPRESS MAIL" mailing label number <u>EU863100789US</u>
Date of Deposit <u>February 17, 2004</u>
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner for Patents, P. O. Box 1450, Alexandria, Virginia 22313-1450.
<u>KATHLEEN A. KUNA</u> (Typed or printed name of person mailing paper or fee)
<u></u> (Signature of person mailing paper or fee)

CASE NO. JJA-0305



27810

PATENT TRADEMARK OFFICE

SYNTHESIS OF STERICALLY HINDERED SECONDARY
AMINOETHER ALCOHOLS FROM ACID
ANHYDRIDE AND/OR ACID HALIDE AND SULFUR TRIOXIDE

5

FIELD OF THE INVENTION

[0001] The present invention relates to a method for the preparation of severely sterically hindered secondary aminoether alcohols which are useful in the removal of hydrogen sulfide from gaseous streams containing hydrogen sulfide and which may also contain carbon dioxide.

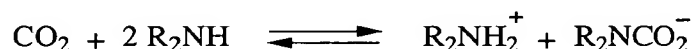
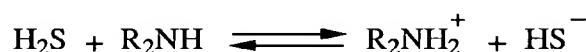
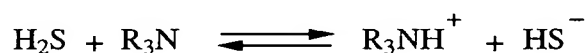
DESCRIPTION OF RELATED ART

[0002] It is well-known in the art to treat gases and liquids, such as mixtures containing acidic gases including CO₂, H₂S, CS₂, HCN, COS and oxygen and sulfur derivatives of C₁ to C₄ hydrocarbons with amine solutions to remove these acidic gases. The amine usually contacts the acidic gases and the liquids as an aqueous solution containing the amine in an absorber tower with the aqueous amine solution contacting the acidic fluid countercurrently. Usually this contacting results in the simultaneous removal of substantial amounts of both the CO₂ and H₂S. USP 4,112,052, for example, utilizes a sterically hindered amine to obtain nearly complete removal of CO₂ and H₂S acid gases. This process is particularly suitable for systems in which the partial pressures of the CO₂ and related gases are low. For systems where the partial pressure of CO₂ is high or where there are many acid gases present, e.g., H₂S, COS, CH₃SH, CS₂, etc., a process utilizing an amine in combination with a physical absorbent, referred to as a "non-aqueous solvent process" is practiced. Such a system is described in USP 4,112,051.

30

[0003] Selective removal of H₂S from acid gas systems containing both H₂S and CO₂, however, is very desirable. Such selective removal results in a relatively high H₂S/CO₂ ratio in the separated acid gas which facilitates the subsequent conversion of the H₂S to elemental sulfur in the Claus process.

5 [0004] The typical reactions of aqueous secondary and tertiary amines with CO₂ and H₂S can be represented as follows:



15 where R is the same or different organic radical and may be substituted with a hydroxyl group. Because the reactions are reversible they are sensitive to the CO₂ and H₂S partial pressures which is determinative of the degree to which the reactions occur.

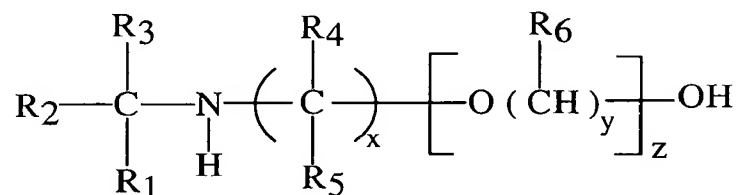
20 [0005] Selective H₂S removal is particularly desirable in systems having low H₂S/CO₂ ratios and relatively low H₂S partial pressures as compared to that of the CO₂. The ability of amine to selectivity remove H₂S in such systems is very low.

25 [0006] Solutions of primary and secondary amines such as monoethanolamine (MEA), diethanolamine (DEA), diisopropanolamine (DPA), and hydroxyethoxyethylamine (DEA) absorb both H₂S and CO₂, and thus have

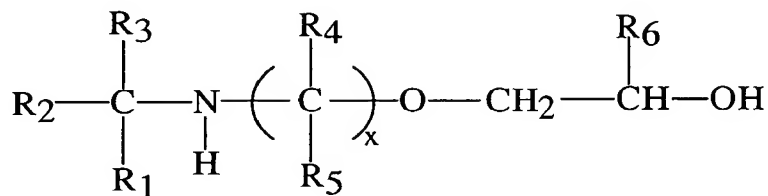
proven unsatisfactory for the selective removal of H₂S to the exclusion of CO₂. The CO₂ forms carbamates with such amines relatively easily.

- 5 [0007] H₂S has been selectively removed from gases containing H₂S and CO₂ by use of diisopropanolamine (DIPA) either alone or mixed with a non-aqueous physical solvent such as sulfolane. Contact times, however, must be kept short to take advantage of the faster reaction of H₂S with the amine as compared to the rate of CO₂ reaction with the amine.
- 10 [0008] Frazier and Kohl, Ind. and Eng. Chem., 42, 2288 (1950) showed that the tertiary amine methyldiethanolamine (MDEA) is more selective toward H₂S absorption as compared to CO₂. CO₂ reacts relatively slowly with tertiary amines as compared to the rapid reaction of the tertiary amine with H₂S. However, it has the disadvantage of having a relatively low H₂S loading
- 15 capacity and limited ability to reduce the H₂S content to the desired level at low H₂S pressures encountered in certain gases.
- [0009] UK Patent Publication No. 2,017,524A discloses the use of aqueous solutions of dialkylmonoalkanolamines, e.g., diethylmonoethanol amine
- 20 (DEAE), for the selective removal of H₂S, such material having higher selectivity and capacity for H₂S removal at higher loading levels than MDEA. DEAE, however, has the disadvantage of a low boiling point of 161°C, making it relatively highly volatile resulting in large material loss.
- 25 [0010] USP 4,471,138 the entire teaching of which is incorporated herein by reference, teaches severely sterically hindered acyclic secondary aminoether alcohols having a high selectivity for H₂S compared to CO₂. Selectivity is maintained at high H₂S and CO₂ loadings.

[0011] The severely sterically hindered acyclic aminoether alcohols of USP 4,471,138 are represented by the general formula:



5 wherein R_1 and R_2 are each independently selected from the group consisting of alkyl and hydroxyalkyl radicals having 1-4 carbon atoms, R_3 , R_4 , R_5 and R_6 are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl radicals having 1-4 carbon atoms, with the proviso that at least one of R_4 or R_5 bonded to the carbon atom which is directly bonded to the nitrogen
10 atom is an alkyl or hydroxyalkyl radical when R_3 is hydrogen, x and y are each positive integers ranging from 2-4, and z is a positive integer ranging from 1-4. These materials are prepared by a high temperature reaction preferably in the presence of a solvent, of a secondary or tertiary alkyl primary amine with an ether alcohol containing a carbonyl functionality in the presence of a source of
15 hydrogen or with a haloalkoxyalkanol. Preferably the composition is of the general formula:



wherein:

$R_1 = R_2 = R_3 = \text{CH}_3-$; $R_4 = R_5 = R_6 = \text{H}$;

$R_1 = R_2 = R_3 = \text{CH}_3-$; $R_4 = \text{H}$ or CH_3 ; $R_5 = R_6 = \text{H}$;

5 $R_1 = R_2 = R_3 = R_6 = \text{CH}_3-$; $R_4 = R_5 = \text{H}$;

$R_1 = R_2 = R_3 = \text{CH}_3\text{CH}_2-$; $R_4 = R_5 = R_6 = \text{H}$; or

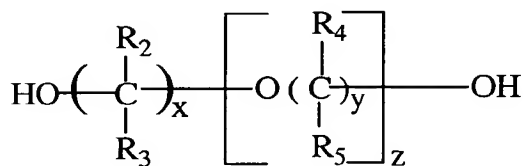
$R_1 \neq R_2 \neq R_3 = \text{H}, \text{CH}_3-, \text{CH}_3\text{CH}_2-$; $R_4 \neq R_5 \neq R_6 = \text{H}, \text{CH}_3-$;

and where $x = 2$ or 3 .

10 **[0012]** U.S. Patent 4,487,967 is directed to a process for preparing severely sterically hindered secondary aminoether alcohols by reacting a primary amino compound with a polyalkenyl ether glycol in the presence of a hydrogenation catalyst at elevated temperatures and pressures. The primary amino compounds employed have a general formula:



where R^1 is selected from the group consisting of secondary or tertiary alkyl radicals having 3 to 8 carbon atoms or cycloalkyl radicals having 3 to 8 carbon atoms. The polyalkenyl ether glycols employed have the general formula



where R_2 , R_3 , R_4 and R_5 are each independently selected from the group consisting of hydrogen, C_1 - C_4 alkyl radicals, and C_3 - C_8 cycloalkyl radicals, with the proviso that if the carbon atom of R_1 directly attached to the nitrogen atom is secondary, at least one of R_2 and R_3 directly bonded to the carbon which is bonded to the hydroxyl group is as alkyl or cycloalkyl radical, x and y are each positive integers independently ranging from 2 to 4 and z is from 1 to 10, preferably 1 to 6, more preferably 1 to 4. The process is carried out in the

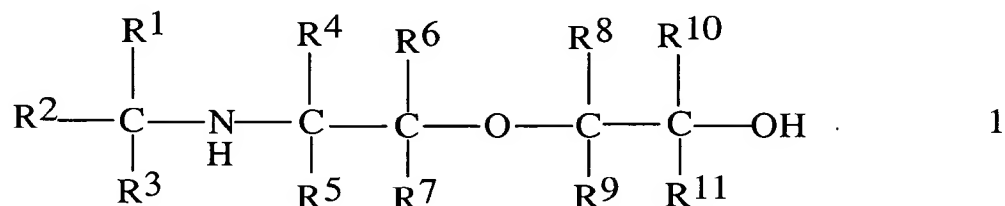
presence of a catalytically effective amount of a supported Group VIII metal containing hydrogenation catalyst at elevated temperatures and pressure and the mole ratio of amino compound to polyalkenyl ether glycol is less than 2:1 when z is greater than 1.

5

SUMMARY OF THE INVENTION

[0013] The present invention is directed to a process for the production of severely sterically hindered secondary aminoether alcohols of the general

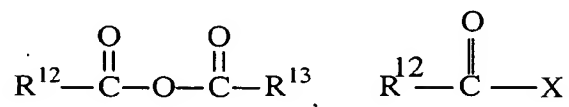
10 formula 1:



wherein R^1 and R^2 are each independently selected from the group consisting of alkyl and hydroxyalkyl radicals having 1 to 4 carbon atoms, preferably 1 to 2 carbon atoms, or R^1 and R^2 in combination with the carbon atom to which they are attached form a cycloalkyl group having 3 to 8 carbons; R^3 is selected from the group consisting of hydrogen, alkyl or hydroxyalkyl radicals having 1 to 4 carbon atoms and mixtures thereof, preferably 1 to 2 carbon atoms, preferably alkyl or hydroxyalkyl radicals having 1 to 4 carbon atoms, more preferably 1 to 2 carbon atoms; R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , and R^{11} are the same or different and are selected from hydrogen, alkyl or hydroxyalkyl radicals having 1 to 4 carbon atoms, preferably 1 to 2 carbon atoms, or cycloalkyl radicals having 3 to 8 carbons; R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , and R^{11} are preferably hydrogen provided that when R^3 is hydrogen at least one of R^4 and R^5 bonded to the carbon directly bonded to the nitrogen is an alkyl or hydroxyalkyl radical, the

25

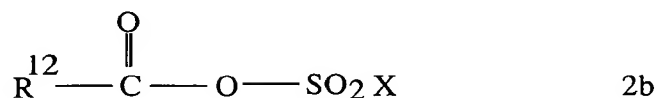
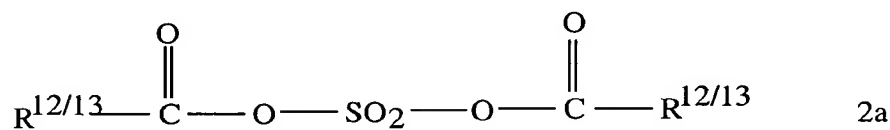
process involving reacting an organic carboxylic acid anhydride or an organic carboxylic acid halide, or mixture thereof, of the formula:



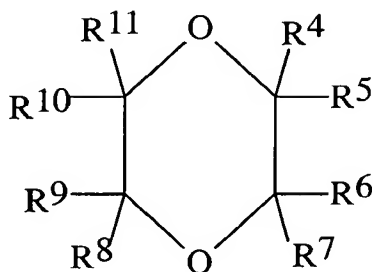
5

wherein R^{12} and R^{13} are the same or different and each is selected from the group consisting of alkyl radicals having 1 to 4 carbon atoms, preferably 1 to 2 carbon atoms, most preferably methyl, aryl radicals, preferably phenyl substituted with hydrogen or alkyl radicals having 1-10 carbon atoms, preferably alkyl radicals having 1-4 carbon atoms, most preferably methyl or hydrogen in the para position, and mixtures thereof, and X is a halogen selected from the group consisting of F, Cl, Br, I, and mixtures thereof, preferably Cl with sulfur trioxide, SO_3 , to yield a mixed sulfonic-carboxylic anhydride or a (mixed anhydride) sulfonyl halide anhydride of the formula 2:

15



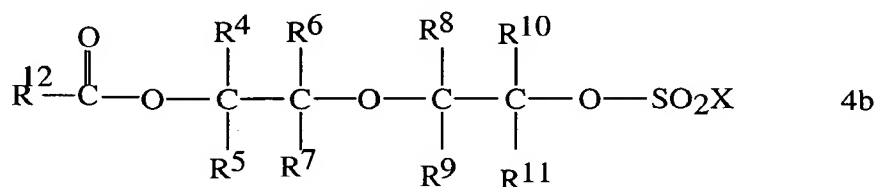
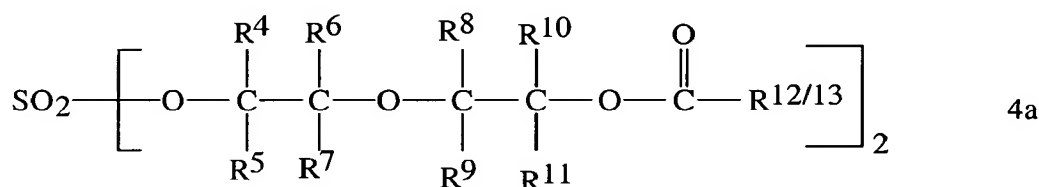
wherein $R^{12/13}$ means that in the product the R group can be R^{12} or R^{13} , or a mixture thereof, which is then reacted with a dioxane of the formula 3:



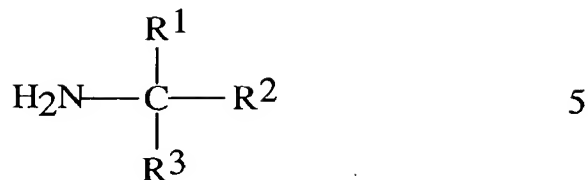
3

20

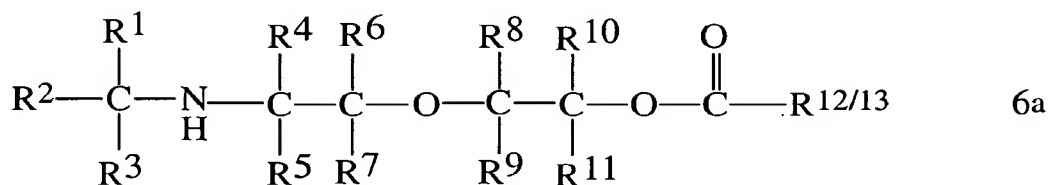
wherein R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, and R¹¹ are the same or different and are selected from hydrogen, alkyl and hydroxyalkyl radicals having 1 to 4 carbons, preferably 1 to 2 carbons or cycloalkyl radicals having 3 to 8 carbons, more preferably R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, and R¹¹ are hydrogen, to yield
 5 cleavage product materials of the general formula 4



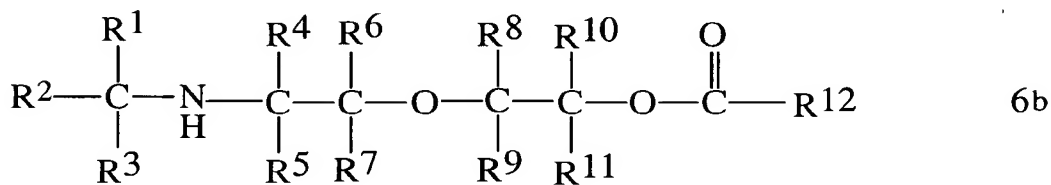
10 or mixtures thereof. It is not necessary that the product from each reaction step be isolated before being reacted with the reactant of a subsequent reaction step up to this point. A cleavage product is still produced. The mixing of the organic carboxylic acid anhydride, organic carboxylic acid halide, or mixture thereof,
 15 with the sulfur trioxide and the dioxane can be in any order or sequence. Thus, the anhydride, acid halide, or mixture thereof, can be mixed with the sulfur trioxide and then mixed with the dioxane, or the dioxane can be first mixed with the sulfur trioxide and then the anhydride, acid halide, or mixture thereof, can be added, or preferably the anhydride, acid halide, or mixture thereof, can be mixed
 20 with the dioxane followed by the addition of the sulfur trioxide. Thus, the combination of the anhydride, acid halide, or mixture thereof, with the dioxane and the sulfur trioxide can be combined into a single reaction mixture and reacted as a mixture resulting in the one step production of the desired cleavage product. This cleavage product is then aminated with an amine of the formula 5:



wherein R^1 , R^2 , and R^3 are as previously defined to yield materials of the general formula 6:



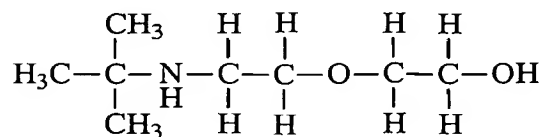
5



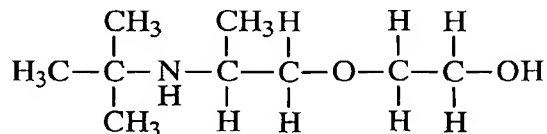
which is subsequently hydrolyzed with a base to yield compound 1.

10

[0014] Preferred compounds defined by the general formula 1 include:

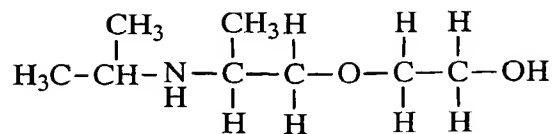


2-(2-*tert*-butylaminoethoxy)ethanol,

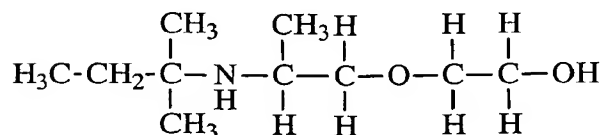


2-(2-*tert*-butylaminopropoxy)ethanol,

15

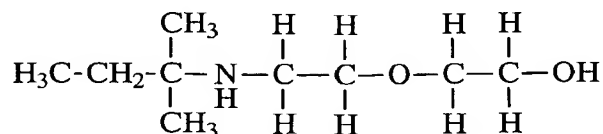


2-(2-isopropylaminopropoxy)ethanol,

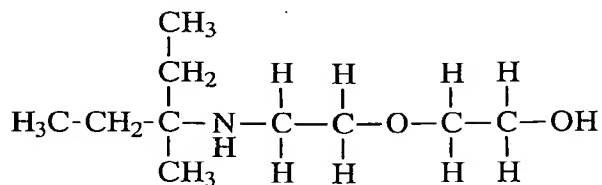


5

2-[2-(1,1-dimethylpropylamino)propoxy]ethanol, or



2-[2-(1,1-dimethylpropylamino)ethoxy]ethanol,

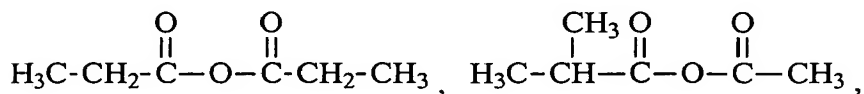


10

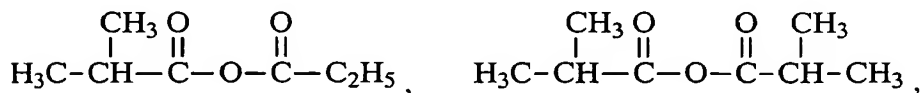
2-[2-(1-ethyl-1-methylpropylamino)ethoxy]ethanol.

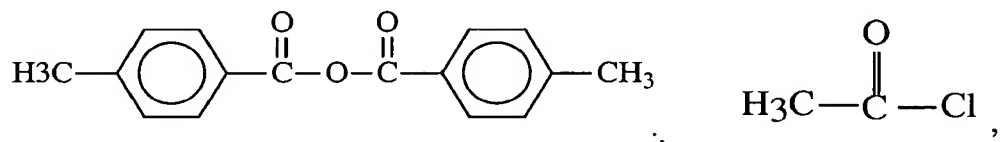
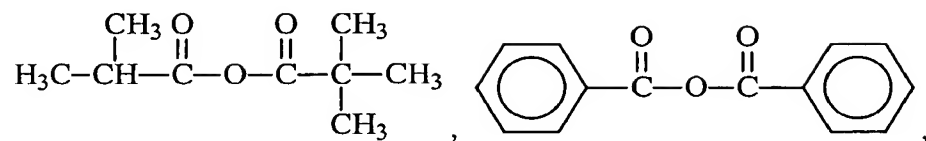
[0015] Typical starting materials are the carboxylic acid anhydrides or carboxylic acid halides of the formula:

15

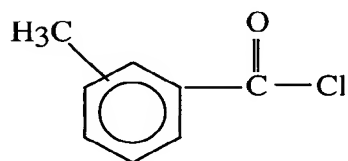
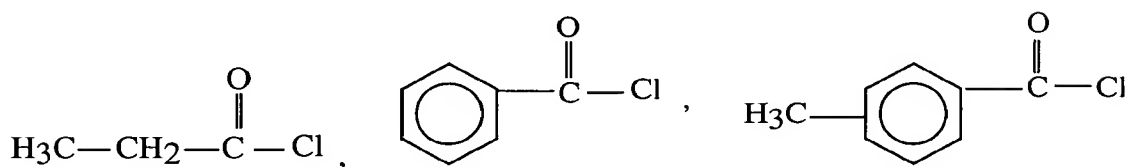


20



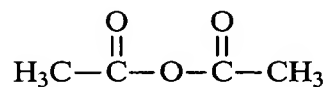


5



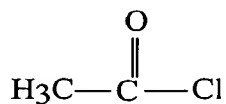
10

Other isomers can be readily envisioned. The preferred anhydride is acetic anhydride:



15

while the preferred acid halide is



20

[0016] The anhydride or acid halide is reacted with sulfur trioxide, SO_3 , to yield a mixed sulfonic-carboxylic anhydride or (mixed anhydride) sulfonyl halide anhydride of general formula 2(a) or 2(b).

[0017] According to the literature, sulfur trioxide reacts with acetic anhydride to form the mixed anhydride diacetyl sulfate **2(a)** wherein $R^{12/13}$ is the CH_3 -radical (80 JCS (P1)) 662-668. Diacetylsulfate (**2(a)**) is a comparatively stable compound at temperatures below $-20^\circ C$ in solution.

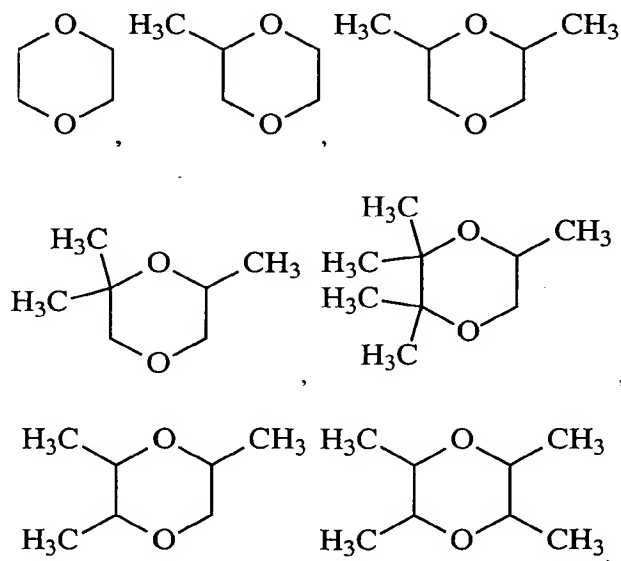
5

[0018] This reaction is performed between about $-70^\circ C$ to about $50^\circ C$, preferably about $-30^\circ C$ to about $25^\circ C$, most preferably between about $-30^\circ C$ to about $0^\circ C$. The reaction can be carried out in an inert solvent such as sulfolane, hexanes, acetonitrile. Preferably the dioxane for the subsequent cleavage reaction is used as the solvent resulting in a unified first step wherein the reaction mixture contains the anhydride, acid halide, or mixture thereof, the sulfur trioxide and the dioxane. This reaction mixture is then reacted under the conditions subsequently described for the dioxane cleavage reaction.

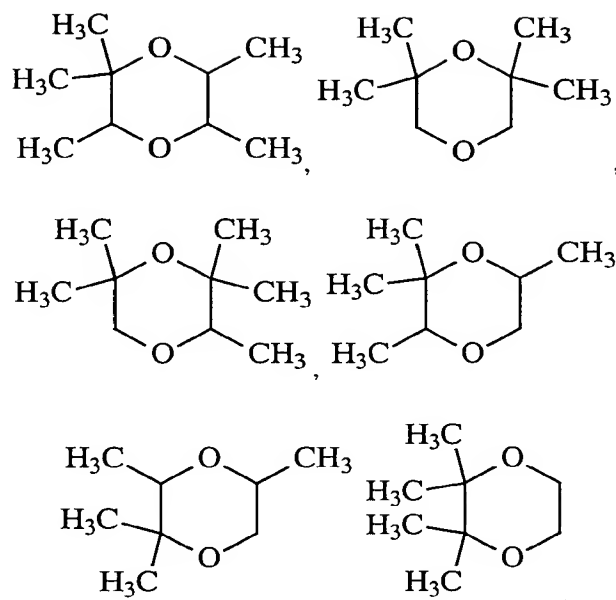
10

15

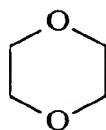
[0019] The mixed sulfonic-carboxylic anhydride **2** is reacted with a dioxane **3** which can be typically of the formula:



20



Other substituted isomers can be readily envisioned. Preferably, the 1,4-dioxane is



[0020] Reaction is for a time sufficient to cleave the dioxane ring and to achieve about 60-90% conversion to product. The dioxane also serves as the solvent for the reaction. The molar ratio of dioxane to sulfonate can range from about 1:1 to about 10:1, preferably about 1:1 to about 8:1, most preferably about 1:1 to about 5:1.

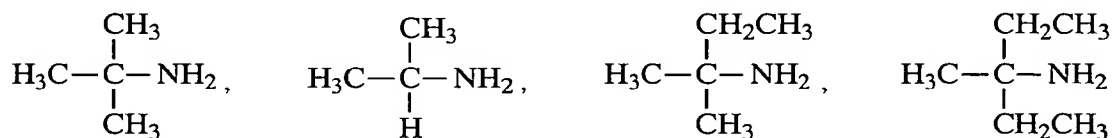
[0021] The cleavage of dioxane is described in greater detail by Karger and Mazur in "The Cleavage of Ethers by Mixed Sulfonic-Carboxylic Anhydrides", Journal of the American Chemical Society, 1968, 90, 3878-3879. See also, "Mixed sulfonic-carboxylic anhydrides. I. Synthesis and thermal stability. New syntheses of sulfonic anhydrides" Journal of Organic Chemistry, 1971, 36, 528, and "Mixed sulfonic-carboxylic anhydrides. II. Reactions with aliphatic ethers and amines" Journal of Organic Chemistry, 1971, 36, 532.

[0022] The reaction can be carried out in the absence of any added solvent e.g., the dioxane serving as the solvent, or an additional solvent such as acetonitrile or toluene can be used, the reaction being conducted at temperatures
5 between about 50°C to about 200°C, preferably about 70°C to about 160°C, more preferably about 80°C to about 140°C.

[0023] Preferably, the reaction is carried out in the absence of any added solvent, the dioxane functioning as both solvent and reactant at a temperature in
10 the range of about 50°C to 200°C, preferably about 70°C to 160°C, more preferably about 80°C to 140°C.

[0024] This cleavage product would then be aminated with an amine **5**, typically of the formula:

15



for a time sufficient to replace the sulfonate group in cleavage product **4** with
20 amine **5**. In general, the amine to sulfonate group mole ratio can be in the range of about stoichiometric to about 10:1, preferably about stoichiometric to about 8:1, more preferably about stoichiometric to about 4:1.

[0025] This amination step can be carried out under any conditions typical in
25 the art. Amination can be conducted at atmospheric or at elevated pressure, elevated pressure being especially suitable when amination is performed using relatively low boiling amines such as *t*-butyl amine.

[0026] This amination can be conducted at pressures of from about
30 atmospheric (1 bar) to about 100 bars, preferably about 1 to about 50 bars, and at

temperatures of from about 40°C to about 200°C, preferably about 40°C to about 125°C. The amination can be performed using reflux, but this is not absolutely necessary. An inert solvent can be optionally used, such as benzene, toluene, diethylether, hexanes, and the like.

5

[0027] Finally, the aminated product **6** is hydrolyzed in a base to yield the final desired product **1**. Typical bases include an alkali metal hydroxide, an alkali metal carbonate, or an alkali metal alkoxide, such as sodium hydroxide, sodium carbonate, sodium methoxide, or sodium tert-butoxide, etc. Mixtures of
10 bases can be used. Reaction is conducted at from about 20°C to about 110°C, preferably about 20°C to about 50°C. The process can be conducted under reflux.

[0028] Use of a solvent is optional for the hydrolysis reaction, one being used
15 if the reactants are not already in the liquid form. Solvents can include water, alcohol and mixtures thereof.

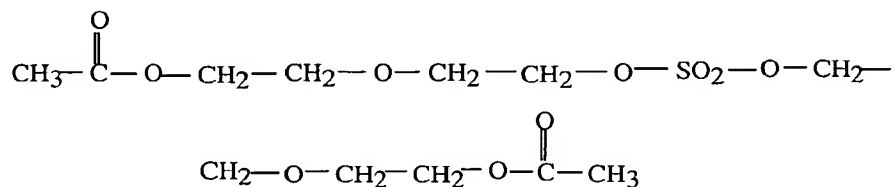
[0029] If alcohols are used, they can be of the same carbon number or are the same alcohols from which the alkoxide bases themselves are derived. Thus,
20 methanol would be a suitable solvent to use where the base is an alkali methoxide.

EXAMPLES

25 Example 1: Sulfur trioxide - acetic anhydride mixture for the cleavage of *p*-dioxane

[0029] Sulfur trioxide (2.5 g, 3 mmol, polymer) and acetic anhydride (3.4 g, 3.15 mL, 33 mmol) were added to 1,4-dioxane (40 mL) at 5°C. The mixture was
30 allowed to warm to room temperature over the course of 1 hour, and stirred at room temperature for 24 hours. No reaction occurred. The reaction mixture was

stirred at 80 to 90°C for 12 hours. Excess dioxane was evaporated in vacuum to give a residue (8 g) as oil. The NMR test of this residue showed a set of signals, some of which can be assigned to the compound.



5

The attempted amination with t-butylamine did not clarify the set of obtained products.

Example 2: Sulfur trioxide-dioxane mixture for reaction with acetic anhydride

10

[0030] Fresh sulfur trioxide from the supplies is a polymer which could not be melted at 36-37°C. A solution of the sulfur trioxide was mixed with excess dioxane at 50-60°C to depolymerize it.

15

[0031] A 100 ml flask was charged with 1,4-dioxane (11 g, 11 mL) under nitrogen and cooled in an ice bath. Sulfur trioxide (1.0 g, 12.5 mmol) was added and the mixture stirred for 30 minutes at room temperature and then for an additional hour at 50-60°C to depolymerize the sulfur trioxide. This mixture was cooled to 5°C. Acetic anhydride (1.43 g, 14 mmol) was added at 5°C and the reaction mixture was stirred at room temperature for one hour. The ¹H NMR spectrum of the mixture showed no characteristic signals corresponding to the cleavage product in the range 3.5-4.2 ppm. The reaction mixture was then refluxed for 12 hours. The ¹H NMR spectrum showed new signals in the range 3.67-3.81 ppm, 4.22-4.28 ppm and 4.49-4.53 ppm which correspond to a mixture of cleavage products.

25

[0032] Separation of the products by column chromatography or silica gel was unsuccessful and only mixtures of unidentified products were isolated.

Example 3: Change of order of reactant addition

5

[0033] A 100 ml flask was charged with 1,4-dioxane (20 g, 20 mL, 0.23 mol) under a nitrogen atmosphere and acetic anhydride (4 mL, 4.2 g, 41 mmol) was added at room temperature. Sulfur trioxide (1.6 g, 20 mmol) was added at 5-10°C. The mixture was stirred for 20 hours at 95-100°C. The ¹H NMR test of
10 the mixture showed the presence of cleavage product in approximately a 1:10 ratio with dioxane.

[0034] Stirring was continued for an additional 12 hours at the same temperature. The ¹H NMR analyses showed the same set of signals.

15

Example 4: Reaction with tert-butylamine

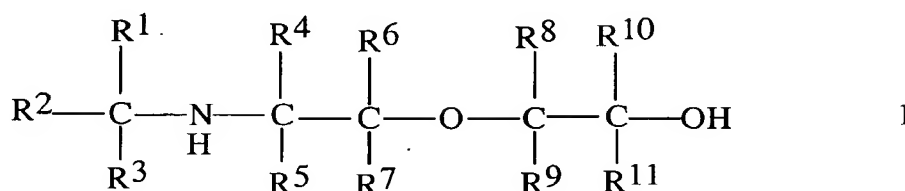
[0035] Because the previously attempted separation of cleavage product was not successful, the crude product from Example 3 was evaporated to dryness and
20 toluene (50 mL) was added to the residual oil. tert-Butylamine (20 mL, 13.92 g, 0.19 mol) was added and the reaction mixture was refluxed for 18 hours. The reaction mixture was cooled to room temperature and washed at room temperature with an aqueous solution of potassium carbonate. Because of the low temperature and short contacting time, this wash with the aqueous solution
25 of potassium carbonate did not result in hydrolysis. The aqueous layer was extracted with diethyl ether. The combined organic layers were evaporated in vacuum to give 3.9 g, approximately 70% purity of aminated product.

Example 5: Hydrolysis with NaOH

[0036] A 2N solution of NaOH in methanol (3 mL, 6 mmol) was added to the aminated product of Example 4 (1 g, 5 mmol) in methanol (5 mL) and the
5 reaction mixture was refluxed for 3 hours. The reaction mixture was evaporated and diethyl ether was added to the residue. A suspension formed which was filtered and the precipitate was washed with diethyl ether. The filtrate was evaporated in vacuum and diethyl ether was added to the residual oil to precipitate sodium salts. This solution was filtered and the solvent was removed
10 in vacuum to recover a yellowish oil (0.9 g). The NMR analysis of this oil showed the desired product, 2-(2-tert butylaminomethoxy)ethanol (EETB) in approximately 90% purity.

WHAT IS CLAIMED IS:

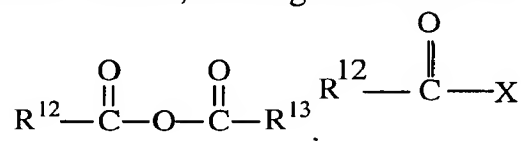
1. A method for the synthesis of severely sterically hindered secondary aminoether alcohols of the formula



5

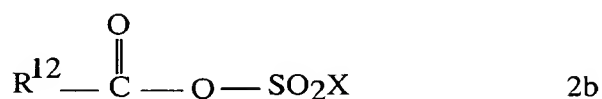
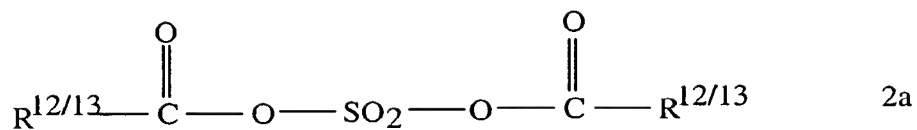
wherein R^1 and R^2 are each selected from the group consisting of alkyl, hydroxylalkyl radicals having 1 to 4 carbon atoms or in combination with the carbon atom to which they are attached they form a cycloalkyl group having 3 to 8 carbon atoms, and R^3 is selected from the group consisting of hydrogen, alkyl or hydroxyalkyl radicals having 1 to 4 carbon atoms, and R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are the same or different and are selected from the group consisting of hydrogen, alkyl and hydroxyalkyl radicals having 1 to 4 carbons provided that at least one of R^4 or R^5 bonded to the carbon atom directly bonded to the nitrogen atom is an alkyl or hydroxyalkyl radical when R^3 is hydrogen, the process involving reacting an organic carboxylic acid anhydride, an organic carboxylic acid halide, or mixture thereof, of the general formula

15

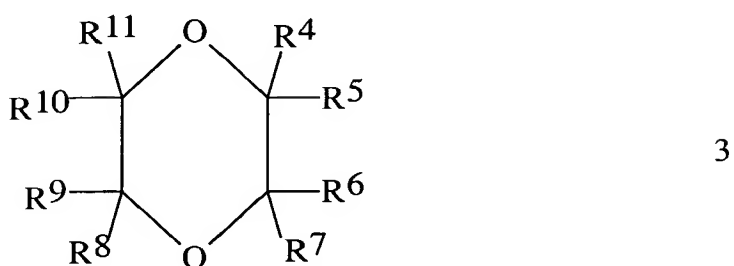


20

wherein R^{12} and R^{13} are the same or different and each is selected from the group consisting of alkyl radicals having 1 to 4 carbon atoms, aryl radicals having hydrogen or C_1 - C_{10} alkyl radicals substituted therein, and mixtures thereof, and X is a halogen selected from the group consisting of F, Cl, Br, I, and mixtures thereof, with sulfur trioxide, SO_3 , to yield a mixed sulfonic-carboxylic anhydride or (mixed anhydride) sulfonyl halide anhydride of formula (2)

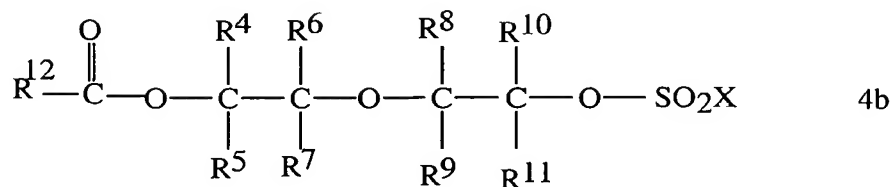
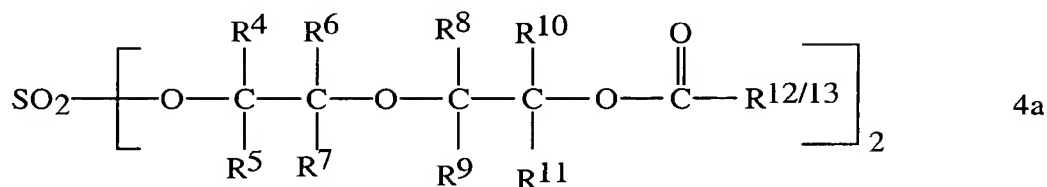


5 which is reacted with a dioxane of formula (3)

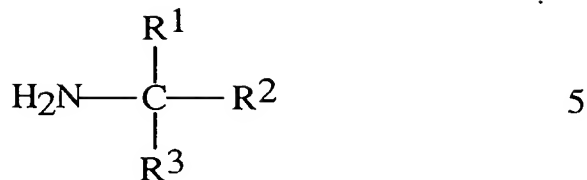


wherein $R^4, R^5, R^6, R^7, R^8, R^9, R^{10}$ and R^{11} are the same or different and are selected from hydrogen, alkyl and hydroxyalkyl radicals having 1 to 4 carbons,

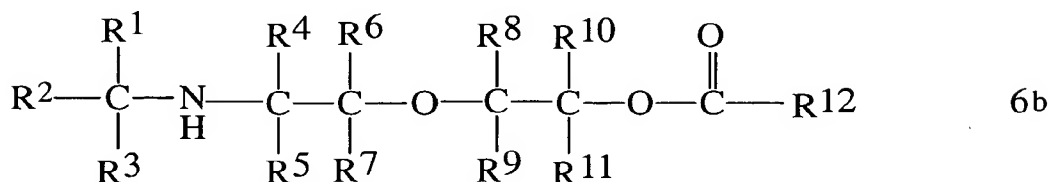
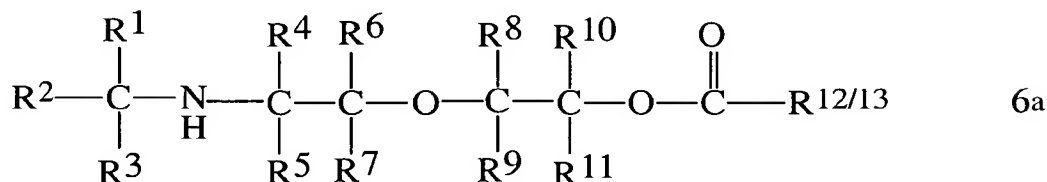
10 to yield



which is then aminated with an alkylamine of the formula



wherein R¹, R² and R³ are as previously defined, to yield (6)



5

which is subsequently hydrolyzed with base to yield product (1).

2. The method of claim 1 wherein R¹, R² and R³ are methyl radicals.

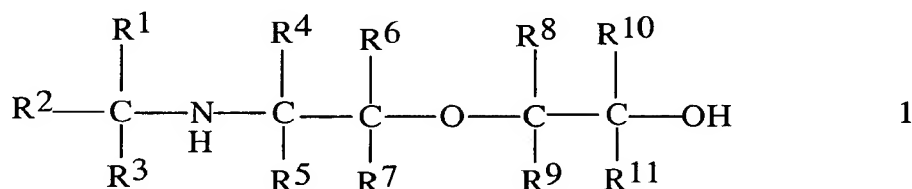
10 3. The method of claim 1 wherein R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are hydrogen.

4. The method of claim 1 wherein R¹² and R¹³ are the same or different and are selected from the group consisting of methyl radical and phenyl with
15 hydrogen or methyl in the para position.

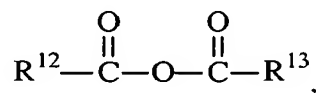
5. The method of claim 1 wherein the base is selected from alkali metal hydroxide, alkali metal alkoxide, or alkali metal carbonate.

6. The method of claim 1 wherein R¹, R² and R³ are methyl and R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are hydrogen.

7. A method for the synthesis of severely sterically hindered secondary aminoether alcohols of the formula

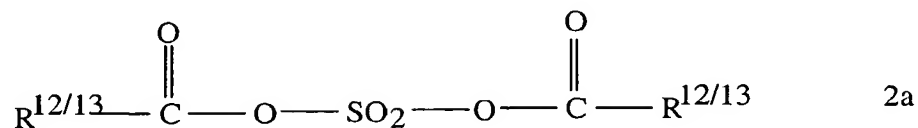


wherein R¹ and R² are each selected from the group consisting of alkyl, hydroxylalkyl radicals having 1 to 4 carbon atoms or in combination with the carbon atom to which they are attached they form a cycloalkyl group having 3 to 8 carbon atoms, and R³ is selected from the group consisting of hydrogen, alkyl or hydroxyalkyl radicals having 1 to 4 carbon atoms, and R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are the same or different and are selected from the group consisting of hydrogen, alkyl and hydroxyalkyl radicals having 1 to 4 carbons provided that at least one of R⁴ or R⁵ bonded to the carbon atom directly bonded to the nitrogen atom is an alkyl or hydroxyalkyl radical when R³ is hydrogen, the process involving reacting an organic carboxylic acid anhydride of the general formula

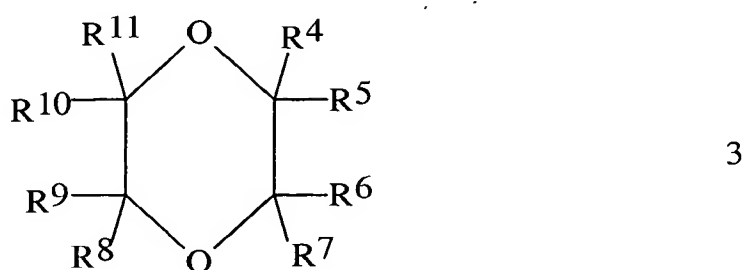


wherein R¹² and R¹³ are the same or different and each is selected from the group consisting of alkyl radicals having 1 to 4 carbon atoms, aryl radicals having hydrogen or C₁-C₁₀ alkyl radicals substituted therein, and mixtures

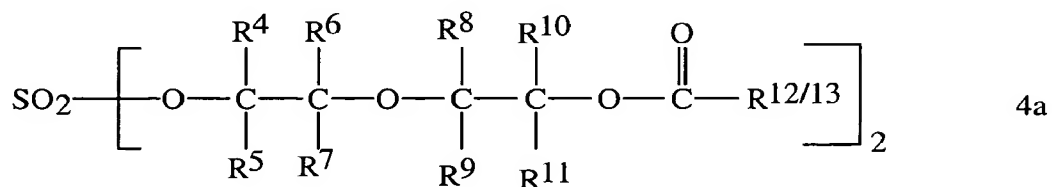
thereof, with sulfur trioxide, SO_3 to yield a mixed sulfonic-carboxylic anhydride of formula (2)



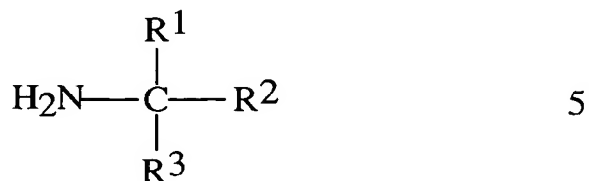
5 which is reacted with a dioxane of formula (3)



wherein $\text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10}$ and R^{11} are the same or different and are
10 selected from hydrogen, alkyl and hydroxyalkyl radicals having 1 to 4 carbons,
to yield

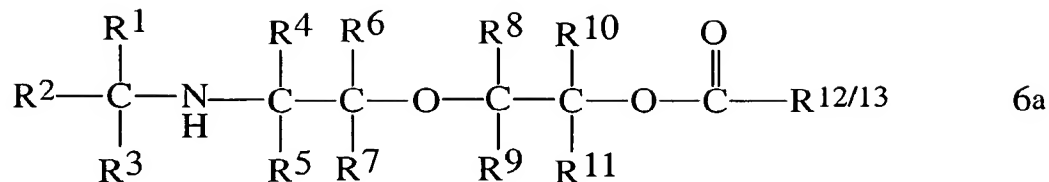


which is then aminated with an alkylamine of the formula



15

wherein R^1, R^2 and R^3 are as previously defined, to yield (6)



which is subsequently hydrolyzed with base to yield product (1).

5 8. The method of claim 7 wherein R^1 , R^2 and R^3 are methyl radicals.

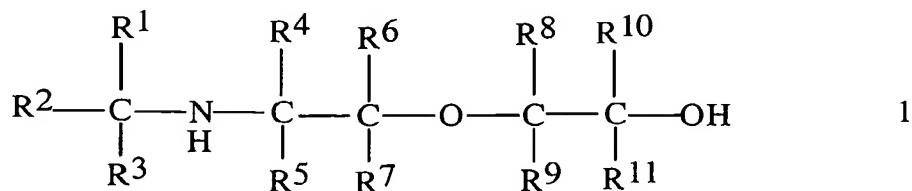
9. The method of claim 7 wherein R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are hydrogen.

10 10. The method of claim 7 wherein R^{12} and R^{13} are the same or different and are selected from the group consisting of methyl radical and phenyl with hydrogen or methyl in the para position.

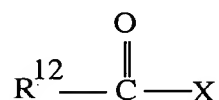
11. The method of claim 7 wherein the base is selected from alkali metal
15 hydroxide, alkali metal alkoxide, alkali metal carbonate.

12. The method of claim 7 wherein R^1 , R^2 and R^3 are methyl and R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are hydrogen.

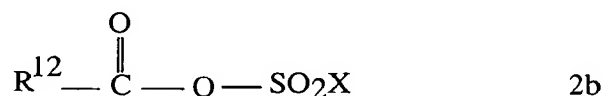
20 13. A method for the synthesis of severely sterically hindered secondary aminoether alcohols of the formula



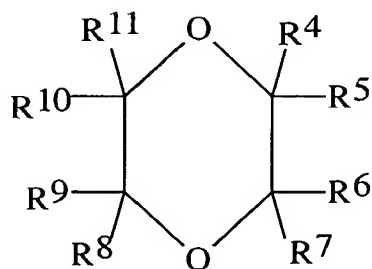
wherein R^1 and R^2 are each selected from the group consisting of alkyl, hydroxylalkyl radicals having 1 to 4 carbon atoms or in combination with the carbon atom to which they are attached they form a cycloalkyl group having 3 to 8 carbon atoms, and R^3 is selected from the group consisting of hydrogen, alkyl or hydroxyalkyl radicals having 1 to 4 carbon atoms, and R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are the same or different and are selected from the group consisting of hydrogen, alkyl and hydroxyalkyl radicals having 1 to 4 carbons provided that at least one of R^4 or R^5 bonded to the carbon atom directly bonded to the nitrogen atom is an alkyl or hydroxyalkyl radical when R^3 is hydrogen, the process involving reacting an organic carboxylic acid halide of the general formula



wherein R^{12} is selected from the group consisting of alkyl radicals having 1 to 4 carbon atoms, aryl radicals having hydrogen or C_1 - C_{10} alkyl radicals substituted therein, and mixtures thereof, and X is a halogen selected from the group consisting of F, Cl, Br, I, and mixtures thereof, with sulfur trioxide, SO_3 to yield (mixed anhydride) sulfonyl halide anhydride of formula (2)

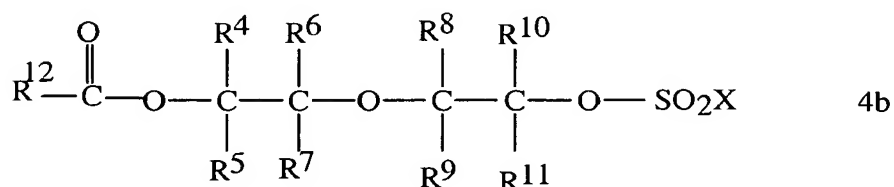


which is reacted with a dioxane of formula (3)

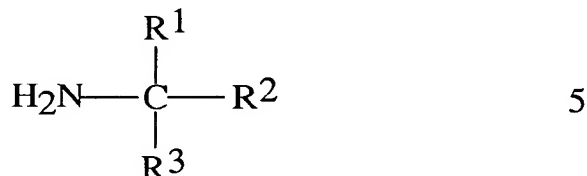


3

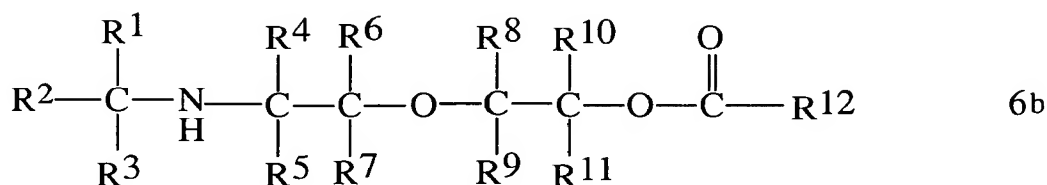
wherein R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are the same or different and are selected from hydrogen, alkyl and hydroxyalkyl radicals having 1 to 4 carbons, to yield



which is then aminated with an alkylamine of the formula



wherein R^1 , R^2 and R^3 are as previously defined, to yield (6)



which is subsequently hydrolyzed with base to yield product (1).

14. The method of claim 13 wherein R^1 , R^2 and R^3 are methyl radicals.

15. The method of claim 13 wherein R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are hydrogen.

16. The method of claim 13 wherein R^{12} and R^{13} are the same or different and are selected from the group consisting of methyl radical and phenyl with hydrogen or methyl in the para position.

17. The method of claim 13 wherein the base is selected from alkali metal hydroxide, alkali metal alkoxide, or alkali metal carbonate.

5 18. The method of claim 13 wherein R^1 , R^2 and R^3 are methyl and R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are hydrogen.

19. The method of claim 1, 7 or 13 wherein the anhydride or acid halide and the SO_3 are reacted at a temperature between about -70° to about $50^\circ C$, the
10 resulting mixed sulfonic-carboxylic anhydride or mixed anhydride sulfonyl halide anhydride (product 2) and the dioxane are reacted at a dioxane to product 2 molar ratio of from about 1:1 to about 10:1 at a temperature of between about $50^\circ C$ to about $200^\circ C$ to produce a cleavage product, the cleavage product and the alkylamine are reacted at an amine to cleavage product ratio ranging from
15 about stoichiometric to about 10:1 at a pressure from about atmospheric (1 bar) to about 100 bars at a temperature of from about $40^\circ C$ to about $200^\circ C$, the resulting aminated product being reacted with base at a temperature from about $20^\circ C$ to about $110^\circ C$.

20 20. The method of claim 1, 7 or 13 wherein the mixing of the anhydride, acid halide, or mixtures thereof, the SO_3 and the dioxane is combined in a single step, the reaction mixture being heated at a temperature of between about $50^\circ C$ to about $200^\circ C$ to produce a cleavage product, the cleavage product and the alkylamine being reacted at an amine to cleavage product ratio ranging from
25 about stoichiometric to about 10:1 at a pressure from about atmospheric (1 bar) to about 100 bars at a temperature of from about $40^\circ C$ to about $200^\circ C$, the resulting aminated product being reacted with base at a temperature from about $20^\circ C$ to about $110^\circ C$.

SYNTHESIS OF STERICALLY HINDERED SECONDARY
AMINOETHER ALCOHOLS FROM ACID
ANHYDRIDE AND/OR ACID HALIDE AND SULFUR TRIOXIDE

5

Abstract of the Disclosure

10

Severely sterically hindered secondary aminoether alcohols are prepared by reacting acid anhydrides or organic carboxylic acid halides with SO_3 to yield a sulfonic carboxylic anhydride compound which is then reacted with a dioxane to cleave the ring of the dioxane yielding a cleavage product which is then aminated with an alkylamine and hydrolyzed with a base to yield

15

the severely sterically hindered secondary aminoether alcohol.